SQUID Magnetometry—Harnessing the Power of Tiny Magnetic Fields

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Measurements associated with the neural currents in the brain can be used to diagnose epilepsy, stroke, and mental illness and to study brain function. One way to observe these tiny electrical currents is to measure the magnetic fields they produce outside the skull—a technique called magnetoencephalography (MEG).

The traditional way to monitor the brain's electrical activity is with EEG, which requires gluing as many as 150 electrodes to the scalp. MEG is a noninvasive technique that measures the direct consequence of neuronal activity in the living brain. MEG, together with EEG, are the only noninvasive techniques of measuring brain function at millisecond time resolution or better. MEG measures brain currents as precisely as EEG does but without physical contact, making it possible to screen large numbers of patients quickly and easily. MEG is also insensitive to the conductivities of the scalp, skull, and brain—which can affect EEG measurements.

Enter the SQUID

Measuring the brain's magnetic fields is not easy, however, because they are so weak. Just above the skull, they have strengths of 0.1 to 1 pT, less than a hundred millionth of the earth's magnetic field. In fact, brain fields can be measured only with the most sensitive magnetic-field sensor known—the superconducting quantum interference device (SQUID).

A SQUID is a loop of superconducting material interrupted by one rf or two dc resistive regions known as Josephson junctions. When cooled to very low temperatures, superconductors conduct electricity without resistance. This lack of resistance allows a SQUID to measure the interference of quantum-mechanical electron waves as the magnetic flux enclosed by the loop changes. A SQUID can measure magnetic fields as small as 1 fT.

Cohen first reported detecting a magnetic signal originating from the human brain in 1968 using a nonsuperconducting sensor.[1] Shortly thereafter, an rf SQUID sensor was used for the first time to measure a biomagnetic signal originating from the human heart,[2] and after only two more years, the same instrument was successfully used to record a human magnetic alpha rhythm with a satisfactory signal-to-noise ratio.[3] The first evoked-response magnetic signals associated with brain activity evoked by peripheral sensory stimulation measured with a SQUID sensor was reported in 1975.[4]

The LANL Superconducting Image Surface Whole-Head MEG System

The LANL SQUID team has designed and built a whole-head MEG system that uses 155 dc SQUIDs to provide simultaneous recordings of MEG activity over the entire head. The SQUIDs become superconducting when immersed in

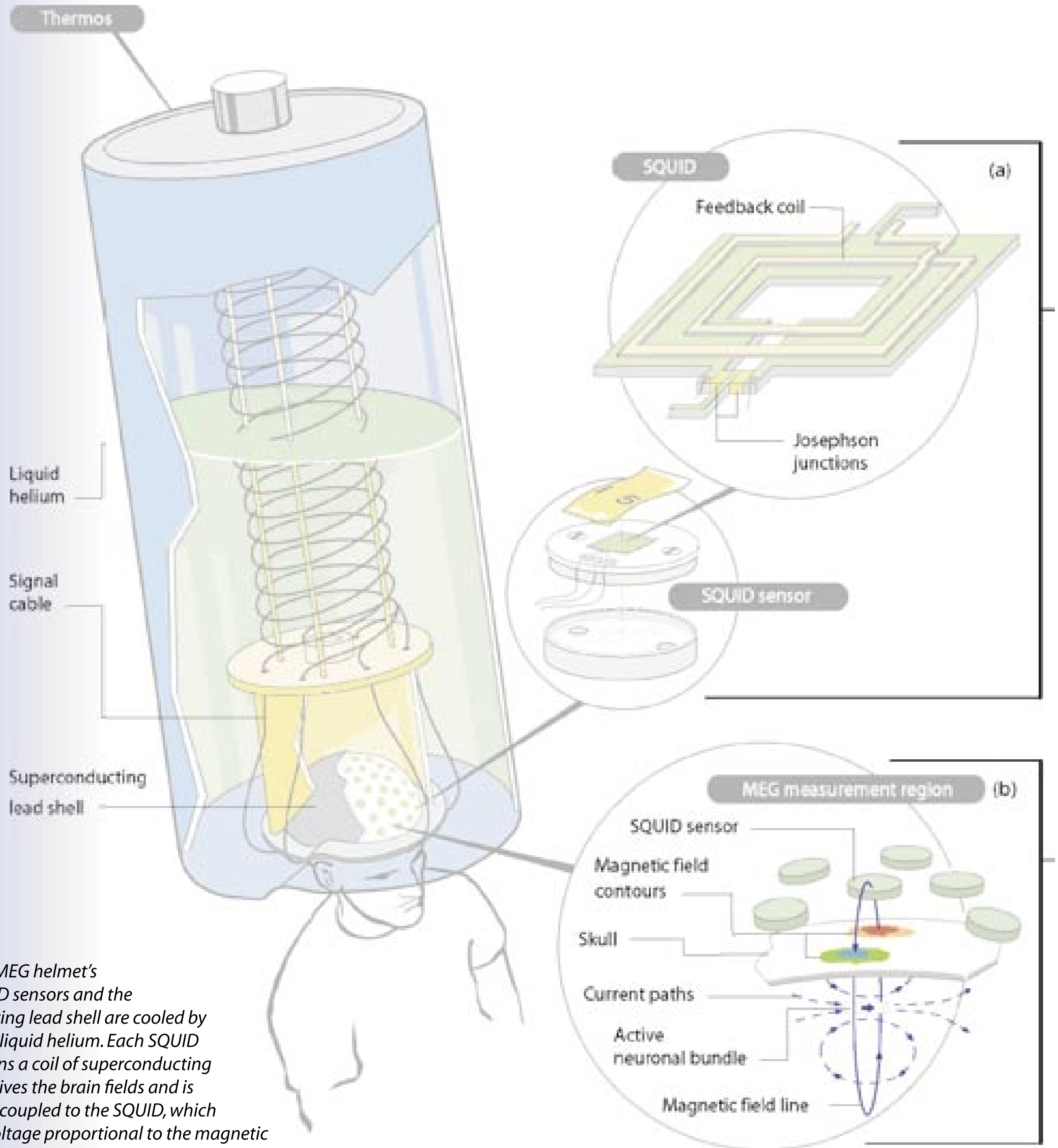

Figure 1. The MEG helmet's array of SQUID sensors and the superconducting lead shell are cooled by immersion in liquid helium. Each SQUID sensor contains a coil of superconducting wire that receives the brain fields and is magnetically coupled to the SQUID, which produces a voltage proportional to the magnetic field received by the coil. A computer program converts the SQUID data into maps of the currents flowing throughout the brain as a function of time. (a) The magnetic field lines that pass through the square hole at the SQUID's center determine the phases of electron waves circulating in the SQUID's superconducting region (green): the waves' interference is proportional to the magnetic flux over the hole. Because superconductors have no electrical resistance, the interference can be measured only by interrupting the superconductor with small regions that have electrical resistance—the two Josephson junctions—so that voltage drops will develop across them. The voltage measured across the junctions is proportional to the magnetic flux over the SQUID's square hole. The feedback coil magnetically couples the SQUID to the pick-up coil in the SQUID sensor. A SQUID is typically 10 to 100 µm on a side. (b) The colored contours show how the magnetic field produced by neural brain currents (dashed arrows) changes in intensity and polarity over the skull's surface. In the red region, the field is most intense in a direction pointing out of the skull. In the blue region, the field is most intense in a direction pointing into the skull.

liquid helium (4 K) contained in a large thermos. The helmet is positioned over a patient's head as he or she sits in a chair (Figure 1).

With sophisticated computer algorithms, MEG data are converted into current maps that give researchers a real-time image of where activity is occurring in the brain. The LANL system responds to brain-current changes in less than a thousandth of a second, adequate for most brain-current studies. The SQUIDs themselves respond in about a millionth of a second. Using specially designed current coils, the LANL MEG system has achieved a spatial resolution of better than 0.25 mm, better than presently reported by any other MEG system (Figure 2).

Eliminating "Noise"

During a MEG measurement, the SQUIDs must be shielded from ambient magnetic fields, whose "noise" tends to swamp the brain signals. Ambient fields are produced mainly by the power lines in a building, although the earth's magnetic field and even the steel in a passing car contribute. (Ferromagnetic materials like steel locally distort the earth's field.) At the frequencies of interest in brain studies—a few to several hundred hertz—the ambient fields must typically be reduced by a factor of 10,000 to 100,000. The helmet's SQUIDs are partially shielded from ambient fields by a thick, hemispherical shell of lead, which becomes superconducting at liquid-helium temperatures. Because superconductors perfectly reflect magnetic fields, the shell reduces ambient fields to as little as one thousandth of their initial strengths. The shielding is not perfect because the shell does not completely enclose the head. The SQUIDs near the shell's crown are better shielded than those near its brim. The shell also reflects the brain's magnetic fields back to the SQUID array, increasing the helmet's sensitivity.

Usually, ambient fields are reduced by taking MEG data in a specially shielded room built with very expensive materials. The superconducting shell effectively blocks magnetic fields from zero to several thousand hertz. Thus, measurements made with the shell require only a "low-end" shielded room, which costs about $100,000—one-fifth that of conventional shielded rooms.

The team has recently added external SQUIDs to the helmet that further reduce the effects of ambient fields. The external SQUIDs measure these fields at several points just outside the superconducting shell, and a computer program then subtracts the fields from the brain-field data to reduce the ambient fields' effects by another factor of 1,000—at all frequencies.

Applications of the MEG/SQUID Technologies

Diagnosing epileptic seizures. For 20% of epilepsy patients, drugs cannot adequately control seizures, and surgically removing the brain tissue where the seizures originate—the epileptigenic tissue—is the only option. But the surgeon must know precisely where the aberrant tissue is to avoid removing nearby tissue required for motor control, sense perception, language, and memory. In addition, by pinpointing how the brain responds to visual, auditory, tactile, or other stimuli, MEG can help

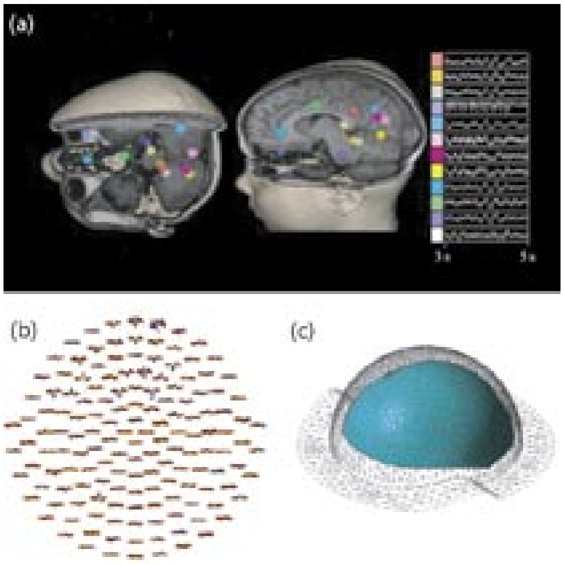

Figure 2. (a) A computer program converts the raw MEG data into maps of the brain's electrical activity as a function of time. These maps can be used to diagnose epilepsy, stroke, and mental disease and to study brain function. (b) The raw data obtained from the 155 SQUID sensors in the MEG helmet. The red waveforms were obtained with the patient's eyes closed. The blue waveforms were obtained as the patient observed a flashing light. (c) The superconducting lead shell. The gray mesh defines the shell's contour. SQUID sensors are attached to the blue surface. At liquid-helium temperatures, the lead shell becomes superconducting and is therefore an excellent magnetic shield. Because a superconductor perfectly reflects magnetic fields at all frequencies, the shell helps shield the underlying SQUID array from ambient magnetic fields. The shell also shields SQUIDs placed outside the shell from the brain's magnetic fields. These external SQUIDs provide data used to help cancel the effects of ambient fields. The superconducting shell and external-field-cancellation method greatly reduce the cost of the magnetically shielded room required for MEG measurements, making them more affordable.

assess the effects of possible collateral damage during surgery.

A brain scan can precisely locate the epileptigenic tissue if the imaging method has high spatial resolution and is fast enough to detect the seizure discharge or the electrical activity that precedes a seizure, which also originates in the epileptigenic tissue. Although seizures occur sporadically, the electrical activity associated with them occurs continually.

Peering into the brain columns. The SQUID team has also developed MicroMEG—using a centimeter-long linear array of SQUIDs with a potential spatial resolution of tens of micrometers. Made of "high-temperature" superconductors, the array's twelve SQUIDs are cooled by liquid nitrogen (77 K) instead of liquid helium (4 K). The MicroMEG array requires less thermal insulation than arrays cooled with liquid helium. Thus, the MicroMEG SQUIDs can be brought within half a millimeter of the tissue under study, allowing extremely high-resolution measurements.

MicroMEG will be used to probe the electrical activity of as few as a few thousand to tens of thousands neurons in one of the brain's cortical columns. The columns are believed to operate in parallel, like the hundreds of microprocessors in a supercomputer that work in parallel to achieve high overall speed. Such studies will improve our understanding of brain function.

Measuring a baby's heartbeat. A variant of MEG called fetal magnetocardiography (FMCG) can be used to diagnose and treat fetal heart conditions. In fact, FMCG is the only way to measure the electrical signals produced by the heartbeat of a baby in the womb. And only the heart's electrical signals contain the detailed timing information required to diagnose and treat fetal arrhythmias. Stethoscopes and ultrasound cannot provide this information because they use sound. Nor is electrocardiography (ECG) useful, because it directly measures the electricity produced by the heart through electrodes taped to the body. However, the baby is electrically insulated from the mother.

Around the twentieth week, the baby's sebaceous glands secrete a waxy, white substance called *vernix caseosa*, which covers the baby's skin to protect it from amniotic fluid in the womb. Because the *vernix* is electrically insulating, electrical signals from the baby's heartbeat cannot pass into the mother's body for measurement on her skin. However, the magnetic fields produced by the baby's heartbeat pass easily through the *vernix* and can be measured with FMCG. Although in principle ECG could be used before the *vernix* forms, the fetal heart is then too small to produce a detectable electrical signal. Unlike other medical diagnostic techniques, FMCG poses no risk to the unborn baby or the mother because it merely receives the magnetic signals sent out by the baby's heart.

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Acknowledgment

Our work was funded by NIH and the DOE Office of Biological and Environmental Research.

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